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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,296	06/21/2001	Thomas E. Tarara	0054.10	6348

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EXAMINER	
GOLLAMUDI, SHARMILA S	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 04/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/886,296	TARARA ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-15, 18-23, 39-47, and 49-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-15,18-23,39-47 and 49-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of the Amendments filed in January 21, 2004 is acknowledged. Claims 4-15, 18-23, 39-47, and 49-56 are pending in this application. Claims 1-3, 16-17, 24-38, and 48 stand cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 49, and 53-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claims recite "fungicides" as an active agent, however the examiner does not find support in the specification of the word fungicide. If the applicant does assert there is support, the applicant is requested to supply the specific page and line in the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 4, 8-15, 18-23, 39-47, 49-50, and 55-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes et al (US 5855913, cited prior art) in view of Cohen et al (5149543) by themselves, or in further view of Yen (5308620, cited prior art).

Hanes et al teach aerodynamically light particles for drug delivery to the pulmonary system. The particles have a tap density of less than 0.4 g/cm3, instant aerodynamic diameter, and a mass mean diameter between 5 to 30 microns (Note abstract and claim 1). Claim 3 teaches a tap density of less than 0.1 g/cm3. Hanes teaches features such as irregular surface texture and porous structure contribute to low tap density and manipulation of these features permits the delivery of larger particle envelope volumes into the lungs (col. 9, lines 10-25). Further, low tap density particles are taught to have small aerodynamic diameter (instant diameter) (col. 9, lines 26-45). The particles contain surfactants such as DPPC (instant gel to liquid temperature) and the microstructures are taught to encapsulate active agents, which allows the active to remain protected (col. 10, lines 37-50 and examples). Biodegradable polymer, copolymers, or a blend may be utilized. Hanes teaches the use of polyglycolic acid and

polylactic acid with a surfactant (DPPC) may be utilized and the polyester may also have a charged or functionizable groups such as amino acids. Other polymers taught are acrylic acids and methacrylic acids and polyvinyl compounds may be used to make the microsphere. See column 5, line 49 to column 6, line 27. Further, the particles may be formed into microspheres by methods such as coacervation, interfacial polymerization, etc. (note col. 6). Instant therapeutic agents are taught on column 10, lines 4-30.

Hanes et al do not teach the use of calcium in the structural matrix.

Cohen et al teach a method of making microspheres. The method is based on the use of water-soluble polymers with charged sides that are crosslinked with multivalent cations (abstract). Suitable polymers that are reacted with cations are polyacrylic acids, polymethacrylic acid, PCPP, polyvinyl compounds, etc (col. 4, lines 1-5). The cations taught are calcium, copper, magnesium, etc (col. 6, line 22).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hanes and Cohen since Cohen teaches the method of making microspheres thorough coacervation using cations such as calcium. One would be motivated to do so with the expectation of similar results since Hanes teaches the use of polymers with charged sides such as polyacrylic acids, etc. and teaches that any process of making the microsphere is suitable.

The manipulation of tap density and pore size are deemed obvious to one of ordinary skill in the art since Hanes teaches the manipulation of surface roughness (porosity), diameter, and tap density determine the delivery site of the particles (col. 8,

lines 19-68). Therefore, one would be motivated to manipulate the factors and fabricate the microstructure according to the region to be targeted.

Response to Arguments

Applicant argues that Hanes et al do not teach an inhalable powder comprising a microstructure containing calcium in the phospholipids. Applicant argues that Hanes et al teach polymer such as polylactic acid and polyglycolic acid and Cohen teaches the use of multivalent polyion to crosslink water-soluble polymers having a charged side chain. It is argued that the preferred polymers in Hanes et al do no teach water-soluble polymers having charged side chains.

Applicant's arguments have been fully considered but they are not persuasive. Firstly, it is pointed out that the phrase "inhalable composition" denotes intended use of the composition and is not given weight since it does not provide a structural limitation to the claims to distinguish it over the art. However, for arguendo sake the examiner points out that Hanes does teach a composition for inhalation. Secondly, it is pointed out that polylactic acid polymers are water-soluble polymers. Furthermore, column 6, lines 13-14 are pointed out wherein Hanes et al clearly suggests that PGA and PLA may have charged or functionalizable groups. Additionally, page 17 of the instant specification is pointed wherein applicant clearly states that charges may be imparted onto the microstructure by charge imparting material such as polyanionic or polycationic material such as *polylactic acid*, polyacrylic acid, etc. Therefore, the examiner is confused by the applicant's assertion that Hanes's polylactic acid is not charged when clearly the applicant has identified this polymer has a charged material at the time of

filing the specification. Thirdly, it is pointed out that Hanes teaches other polymer in addition to PLA and PGA, for instance Hanes teaches the use of polyacrylic, methacrylic polymers, and polyvinyl compounds. Therefore, since Hanes teaches the formation of microstructures utilizing conventional methods known in the art such as simple and complex coacervation, it is the examiner's position that a skilled artisan would look to Cohen et al's teachings of making microstructures utilizing coacervation. Further, Cohen et al teach the use of cations such as calcium to react with polymers, such as those taught in Hanes. Thus, there is a reasonable expectation of success.

For the reasons stated above, the rejection is maintained.

Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes et al (US 5855913, cited prior art) in view of Cohen et al (5149543) in further view of Yen (5308620).

As set forth above, Hanes et al teach dry powder inhaler compositions. Hanes teaches several active agents including antibiotics in the composition. Cohen et al teach the use of calcium to make a polymer microcapsule.

The references do not specify the pore size.

Yen teaches the method of making stable, porous nanomatrixes. Yen teaches the advantages the porous nature of a carrier vesicle such as this structure allows the substrate of the biologically active molecules to diffuse into the interior of the nanomatrix and for the reaction products to diffuse out. The drugs can also diffuse out of the nanomatrix at rates dependent on the porosity of the nanomatrix carrier. (Note col. 8, lines 34-46).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hanes et al, Cohen et al, and Yen et al and use instant pore size. One would be motivated to manipulate the pore size is to control the rate of the release of actives from the carrier as taught by Yen; therefore depending on the drug used and the desired rate of release, one would be motivated to manipulate its size.

Response to Arguments

Applicants do not completely address the instant rejection. Applicant argues that the claims are not rendered unpatentable for the same reasons as above. Applicant also argues that the claims recite a microstructure, which is hollow and porous.

Applicant's arguments have been fully considered but they are not persuasive. Firstly, it is pointed out that Hanes et al and instant claims recite the same properties of geometric diameter, tap density, and aerodynamic diameter. It is pointed out that tap density is related to the hollowness of the structure. Furthermore, Hanes not only teaches a porous structure, Hanes teaches the manipulation of porosity to decrease tap density depending on the targeted location and since Hanes teaches the instant tap density, it is implicit that both have the same porosity. However, if applicant argues that this is not the case, it is still the examiner's position that Hanes provides adequate guidance to an artisan to manipulate the porosity of the structure. For instance, example 2 teaches that the porosity and surface texture may be increased or decreased by varying inlet and outlet temperatures when spray drying the particles. The motivation to manipulate this factor being that Hanes teaches a porous structure allows for a smaller

tap density. The examiner relies on Yen et al to provide further motivation to manipulate the pore size. Since Hanes teaches the use of the particles for controlled release and Yen teaches that the pores control the rate of release out of a matrix carrier, one would be motivated to manipulate the actual size of the pore depending on the drug utilized and the rate of release. It is the examiner's position that these are manipulatable parameters done during routine optimization and is known to those skilled in the art.

Claim 51-52 under 35 U.S.C. 103(a) as being unpatentable over Hanes et al (US 5855913) in view of Cohen et al (5149543) in further view of Igarashi et al (4201774).

As set forth above, Hanes et al teach dry powder inhaler compositions. Hanes teaches several active agents including antibiotics in the composition.

Hanes does not teach the specific use of aminoglycoside antibiotic.

Igarashi et al teaches aminoglycoside antibiotics for the treatment of gram-positive and gram-negative bacteria. Further, the reference teaches the use diluents such as calcium carbonate for the composition and the composition in a form of an inhalant (col. 5, lines19-40).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the instant medicament in Hanes et al's composition. One would be motivated to do so since the instant antibiotics treat gram-positive and gram-negative bacteria and depending on the patient's requirement, the appropriate drug is used.

Response to Arguments

Applicant does not specifically address the instant rejection. Therefore, the rejection is maintained for the reasons stated above.

Claims 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes et al (US 5855913) in view of Cohen et al (5149543) in further view of Benson et al (5,006,343).

As set forth above, Hanes et al teach dry powder inhaler compositions. Hanes teaches several active agents in the composition.

Hanes does not teach the specific use of fungicides.

Benson et al teach pulmonary administration of active agents to treat pulmonary diseases. Suitable drugs that may be administered for lung specific disease include fungicides. See column 10, lines 33-45.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a fungicide in Hanes et al's composition. One would be motivated to do so since Benson et al teach the use of array of medications including fungicides that are useful for treating lung diseases. Therefore, one would be motivated to utilize the drug of choice depending on the symptoms and diseases being treated.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-242-0614. The examiner can normally be reached on M-F (8:00-5:00) with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SSG

April 3, 2004

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